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M is a DOTA chelator comprising a Gd(III) paramagnetic metal ion;
R₂₆ and R₂₇ are alkyl linker groups;
R₂₈ is the peptide blocking moiety PMALWMR; and,
n is an integer.

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Please add the following new claim:

30. (New) An MRI agent according to claim 23 wherein said peptide is selected from the group comprising PELR (SEQ ID NO: 8), PLGLAR (SEQ ID NO: 9), PGLWA-(D-arg) (SEQ ID NO: 10), PMALWMR (SEQ ID NO: 11), and PMGLRA (SEQ ID NO: 12).

REMARKS

Claims 12-23 and 25-30 are pending. Claim 29 has been amended to elect PMALWMR as the specific peptide blocking moiety. Support for newly added claim 30, is found in cancelled claim 24. An Appendix of Pending Claims is attached for the Examiner's convenience.

The Restriction Requirement dated 9/27/02 required the Applicants to elect a single disclosed species from Claim 24. The five species disclosed in Claim 24 were restricted into five of the six restriction groups cited by the Examiner. Applicants interpreted this to mean that if they elected Group VI, drawn to a blocking moiety other than those of Groups I-V, they would be allowed to prosecute a claim drawn to a generic peptide blocking moiety.

The Examiner's current position as set forth in the Communication dated 1/21/03 is that Applicants must elect a specific peptide blocking moiety. This election requires Applicants to elect a group other than Group VI. Accordingly, Applicants respectfully request that the election of Group VI made in the response to the Restriction Requirement dated 9/27/02 be changed to Group IV, claims 12-24, drawn to a PMALWMR blocking moiety. Claim 24 has been reinstated as new claim 30.

Applicants respectfully assert the election of a peptide blocking moiety imposed by the Examiner is erroneous. Within the context of the claims and the restriction presently imposed, it would be difficult, if not impossible to obtain a claim as broad as claim 29 which is directed to the use of activatable MRI agents comprising a peptide

blocking moiety. By forcing the Applicants to elect a species within the "genus" of "peptide blocking moieties", it is applicants understanding that this would be the broadest claim possibly allowable in the case due to the restriction imposed. If this is not the case and applicants can have the full genus for "peptide blocking moieties" examined in this case via examination of the other types of "peptide blocking moieties" of Groups I through Group V imposed in the Restriction Requirement mailed September 27, 2002 (after an indication of allowability of claims using a single peptide blocking moiety), applicants will withdraw its objection.

Attached hereto is a marked-up version of the changes made to the claims by the "Amendment". The attached page is captioned "**Version with markings to show changes made.**"

Please direct further questions in connection with this Application to the undersigned at (415) 781-1989.

Dated: 2/21/03

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Respectfully submitted,
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Filed under 37 C.F.R. § 1.34(a)

Version with Markings to Show Changes Made

Claim 29 has been amended as follows:

29. (Amended) An MRI agent according to claim 12, 13, or 14 wherein

~~~~~ is a dextran polymer;

M is a DOTA chelator comprising a Gd(III) paramagnetic metal ion;

R<sub>26</sub> and R<sub>27</sub> are alkyl linker groups;

R<sub>28</sub> is a the peptide blocking moiety PMALWMR; and,

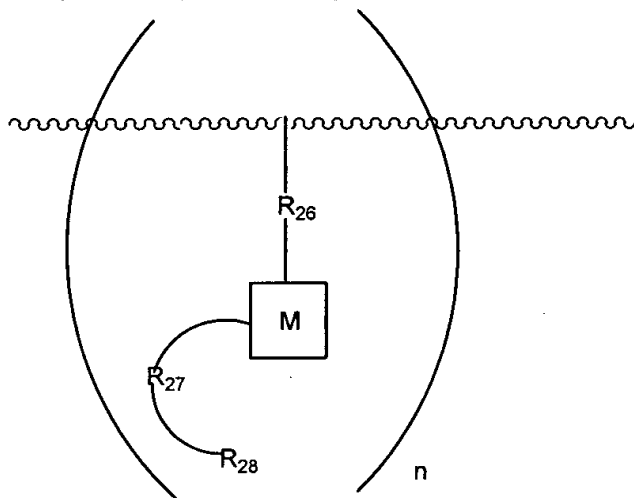
is an integer.

## Appendix of Pending Claims

12. A composition comprising:

- a) a polymer;
- b) at least one MRI agent comprising:
  - i) at least one chelator comprising a paramagnetic metal ion; and,
  - ii) a blocking moiety covalently attached to said chelator which hinders the rapid exchange of water in the remaining coordination sites, wherein said blocking moiety will interact with a target substance such that the exchange of water in the remaining coordination sites is increased; and
- c) a linker group attaching said MRI agent to said polymer.

13. (Amended) An MRI agent according to claim 12 having the formula comprising:



wherein

~~~~~ is a polymer

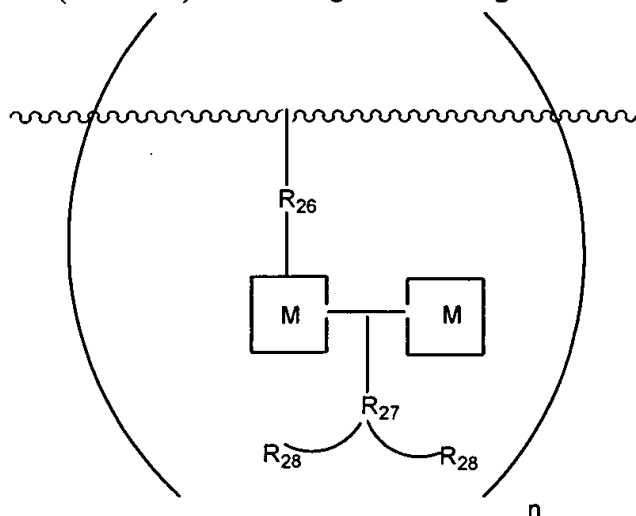
M is a chelator comprising a paramagnetic metal ion;

R₂₆ and R₂₇ are linker groups;

R₂₈ is a blocking moiety; and,

n is an integer.

14. (Amended) An MRI agent according to claim 12 having the formula comprising:



wherein

~~~~~ is a polymer;

M is a chelator comprising a paramagnetic metal ion;

R<sub>26</sub> and R<sub>27</sub> are linker groups;

R<sub>28</sub> is a blocking moiety; and

n is an integer.

15. (Amended) An MRI agent according to claims 12, 13, or 14 wherein said paramagnetic metal ion is selected from the group comprising gadolinium III (Gd<sup>+3</sup> or Gd(III)), iron III (Fe<sup>+3</sup> or Fe(III)), manganese II (Mn<sup>+2</sup> or Mn(II)), dysprosium (Dy<sup>+3</sup> or Dy(III)), or chromium (Cr<sup>+3</sup> or Cr(III)).

16. An MRI agent according to claim 15 where said paramagnetic ion is Gd(III).

17. (Amended) An MRI agent according to claims 12, 13 or 14 wherein said linker groups are alkyl groups.

18. An MRI agent according to claim 17 wherein said alkyl groups are substituted alkyl groups.

19. (Amended) An MRI agent according to claims 12, 13 or 14 wherein said linker groups are aryl groups.

20. An MRI agent according to claims 19 wherein said aryl groups are substituted aryl groups.

21. (Amended) An MRI agent according to claims 12, 13 or 14 wherein at least one of said linker groups are selected from the group comprising p-aminobenzyl, methyl, ethyl, propyl, butyl, pentyl, hexyl, propionic acid, aminobutyl, p-alkyl phenols, and 4-alkylimidazole.

22. (Amended) An MRI agent according to claims 12, 13 or 14 wherein said blocking moiety is a peptide.

23. (Amended) An MRI agent according to claim 22 wherein said peptide binds to a metalloproteinase.

25. (Amended) An MRI agent according to claims 12, [2]13, or [3]14 wherein said polymer is selected from the group comprising functionalized dextrans, styrene polymers, polyethylene, polyanionic polymers, polycationic polymers, and mixed polymers.

26. An MRI agent according to claim 25 wherein said polycation is polylysine.

27. (Amended) An MRI agent according to claim 12, 13, or 14 wherein said polymer comprises a plurality of said MRI agents.

28. (Amended) A method of magnetic resonance imaging of a cell, tissue or patient comprising administering an MRI agent according to claim 12, 13, or 14 to a cell, tissue or patient and rendering a magnetic resonance image of said cell, tissue or patient.

29. (Amended) An MRI agent according to claim 12, 13, or 14 wherein

~~~~~ is a dextran polymer;

M is a DOTA chelator comprising a Gd(III) paramagnetic metal ion;

R₂₆ and R₂₇ are alkyl linker groups;

R₂₈ is the peptide blocking moiety PMALWMR; and,

n is an integer.

30. (New) An MRI agent according to claim 23 wherein said peptide is selected from the group comprising PELR (SEQ ID NO: 8), PLGLAR (SEQ ID NO: 9), PGLWA-(D-arg) (SEQ ID NO: 10), PMALWMR (SEQ ID NO: 11), and PMGLRA (SEQ ID NO:12).